

AMENDMENT

U.S. Appln. No. 09/429,003

diagnosing or identifying a disease or stage thereof in a eukaryotic organism comprising the steps of:

- e'
- (a) isolating mRNA from cells of one or more eukaryotic organisms which are known to have said disease or a stage thereof (diseased sample), wherein said cells have not contacted the area of said disease and are obtained from a part of said organism distant to the area of said disease, wherein the resulting isolated mRNA is optionally subjected to reverse transcription to obtain isolated cDNA;
 - (b) isolating mRNA from corresponding cells of one or more corresponding normal eukaryotic organisms (normal sample), wherein the resulting isolated mRNA is optionally subjected to reverse transcription to obtain isolated cDNA;
 - (c) separating, by a non-sequence based separation technique, mRNA species or cDNA species present within each of the resulting isolated mRNA or isolated cDNA of step (a) and step (b), wherein the resulting separated mRNA species are optionally subject to reverse transcription to obtain separated cDNA species;
 - (d) selecting between 10 and 500 mRNA species or between 10 and 500 cDNA species from the resulting separated mRNA species or resulting separated cDNA species obtained in step (c), respectively, which are present at a different

AMENDMENT

U.S. Appln. No. 09/429,003

E1
cont
level in the normal sample than in the diseased sample by identifying a signal corresponding to each mRNA species or cDNA species, wherein the resulting selected between 10 and 500 mRNA species are optionally subjected to reverse transcription to obtain between 10 and 500 selected cDNA species; and

- (e) isolating the resulting between 10 and 500 selected mRNA species or resulting between 10 and 500 selected cDNA species obtained in step (d) to obtain isolated selected mRNA species or isolated selected cDNA species, wherein the resulting isolated selected mRNA species are optionally subjected to reverse transcription to obtain isolated selected cDNA species.

E2
Claim 39. (Amended) The method as claimed in Claim 56, wherein, prior to immobilizing in step (f), the resulting isolated selected mRNA species or isolated selected cDNA species of step (e) are amplified.

E3
Claim 47. (Amended) The method as claimed in Claim 56, wherein said solid support is a filter.

Claim 56. (Amended) A method of preparing a gene transcript pattern probe kit comprising the steps of:

- E4
(a) isolating mRNA from cells of one or more eukaryotic organisms which are known to have a disease or a stage thereof (diseased sample), wherein said cells have not contacted the area of said disease and are obtained from a part of said

AMENDMENT

U.S. Appln. No. 09/429,003

Ey
organism distant to the area of said disease,
wherein the resulting isolated mRNA is optionally
subjected to reverse transcription to obtain
isolated cDNA;

- cont
- (b) isolating mRNA from corresponding cells of one or more corresponding normal eukaryotic organisms (normal sample), wherein the resulting isolated mRNA is optionally subjected to reverse transcription to obtain isolated cDNA;
 - (c) separating, by a non-sequence based separation technique, mRNA species or cDNA species present within each of the resulting isolated mRNA or isolated cDNA of step (a) and step (b), wherein the resulting separated mRNA species are optionally subject to reverse transcription to obtain separated cDNA species;
 - (d) selecting between 10 and 500 mRNA species or between 10 and 500 cDNA species from the resulting separated mRNA species or resulting separated cDNA species obtained in step (c), respectively, which are present at a different level in the normal sample than in the diseased sample by identifying a signal corresponding to each mRNA species or cDNA species, wherein the resulting selected between 10 and 500 mRNA species are optionally subjected to reverse transcription to obtain between 10 and 500 selected cDNA species;

AMENDMENT

U.S. Appln. No. 09/429,003

- E4
cont
- (e) isolating the resulting between 10 and 500 selected mRNA species or resulting between 10 and 500 selected cDNA species obtained in step (d) to obtain isolated selected mRNA species or isolated selected cDNA species, wherein the resulting isolated selected mRNA species are optionally subjected to reverse transcription to obtain isolated selected cDNA species; and
 - (f) immobilizing the resulting isolated selected mRNA species or isolated selected cDNA species of step (e) on at least one solid support so as to form a gene transcript pattern probe kit.

Claim 57. (Amended) A method of preparing a standard gene transcript pattern characteristic of a disease or stage thereof of a eukaryotic organism comprising the steps of:

- (a) isolating mRNA from cells of one or more eukaryotic organisms known to have said disease or a stage thereof, (diseased sample) wherein said cells have not contacted the area of said disease and are obtained from a part of said organism distant to the area of said disease, wherein the resulting isolated mRNA is optionally subjected to reverse transcription to obtain isolated cDNA;
- (b) hybridizing the resulting isolated mRNA or isolated cDNA of step (a) to between 10 and 500 mRNA species which are present at a different level in cells in a normal sample than

AMENDMENT

U.S. Appln. No. 09/429,003

84
cont

corresponding cells in a diseased sample, wherein the between 10 and 500 mRNA species or cDNA species are specific for said disease or stage thereof and wherein said cells have not contacted the area of said disease and are obtained from a part of said organism distant to the area of said disease, or to between 10 and 500 cDNA species transcribed from said mRNA species, wherein said mRNA or cDNA species are immobilized on a solid support; and

- (c) assessing the amount of hybridisation so as to obtain said standard gene transcript pattern.

Claim 58. (Amended) A method of preparing a test gene transcript pattern for a disease or stage thereof comprising the steps of:

- (a) isolating mRNA from cells of a test eukaryotic organism, wherein said cells have not contacted the area of said disease and are obtained from a part of said organism distant to the area of said disease, wherein the resulting isolated mRNA is optionally subjected to reverse transcription to obtain isolated cDNA;
- (b) hybridizing the resulting isolated mRNA or isolated cDNA of step (a) to between 10 and 500 mRNA species which are present at a different level in cells in a normal sample than corresponding cells in a diseased sample, wherein the between 10 and 500 mRNA species or cDNA

AMENDMENT

U.S. Appln. No. 09/429,003

E4
cat
species are specific for said disease or stage thereof and wherein said cells have not contacted the area of said disease and are obtained from a part of said organism distant to the area of said disease, or to between 10 and 500 cDNA species transcribed from said mRNA species, wherein said mRNA or cDNA species are immobilized on a solid support, and assessing the amount of hybridization so as to obtain said test gene transcript pattern.

Claim 59. (Amended) A method of diagnosing or identifying a disease or stage thereof in a test eukaryotic organism comprising the steps of:

- (a) isolating mRNA from cells of a test eukaryotic organism, wherein said cells have not contacted the area of said disease and are obtained from a part of said organism distant to the area of said disease, wherein the resulting isolated mRNA is optionally subjected to reverse transcription to obtain isolated cDNA;
- (b) hybridizing the resulting isolated mRNA or isolated cDNA of step (a) to between 10 and 500 mRNA species which are present at a different level in cells in a normal sample than corresponding cells in a diseased sample, wherein the between 10 and 500 mRNA species or cDNA species are specific for said disease or stage thereof and wherein said cells have not contacted

AMENDMENT

U.S. Appln. No. 09/429,003

the area of said disease and are obtained from a part of said organism distant to the area of said disease, or to between 10 and 500 cDNA species transcribed from said mRNA species, wherein said mRNA or cDNA species are immobilized on a solid support;

E4
C1.

- (c) assessing the amount of hybridization so as to obtain a hybridization pattern;
- (d) comparing the resulting hybridization pattern obtained in step (c) with a hybridization pattern obtained by hybridizing isolated mRNA or isolated cDNA prepared from corresponding cells from one or more corresponding eukaryotic organisms known to have said disease or stage thereof to the between 10 and 500 mRNA species or between 10 and 500 cDNA species transcribed from said mRNA species, wherein said mRNA species or cDNA species are immobilized on a solid support; and
- (e) assessing the amount of hybridization, so as to determine the degree of correlation indicative of the presence of said disease or stage thereof, and so as to diagnose or identify said disease or a stage thereof in said test eukaryotic organism.

Claim 60. (Amended) The method as claimed in Claim 57, wherein said organism is human.

Claim 61. (Amended) The method as claimed in Claim 57, wherein said disease is cancer.

AMENDMENT

U.S. Appln. No. 09/429,003

E4
CW
Claim 62. (Amended) The method as claimed in Claim 57, wherein said cells are isolated from tissue, body fluid or body waste of said eukaryotic organism.

E5
Claim 64. (Amended) The method as claimed in Claim 57, wherein said disease is selected from the group comprising stomach, lung, breast, prostate gland, bowel and skin cancer.

Claim 65. (Amended) The method as claimed in Claim 57, wherein said disease is Alzheimer's disease.

← Please add the following new claims: →

E6
-- Claim 66. The method as claimed in Claim 58, wherein said organism is human.

Claim 67. The method as claimed in Claim 58, wherein said disease is cancer.

Claim 68. The method as claimed in Claim 58, wherein said cells are isolated from tissue, body fluid or body waste of said eukaryotic organism.

Claim 69. The method as claimed in Claim 68, wherein said body fluid is blood.

Claim 70. The method as claimed in Claim 58, wherein said disease is selected from the group comprising stomach, lung, breast, prostate gland, bowel and skin cancer.

Claim 71. The method as claimed in Claim 58, wherein said disease is Alzheimer's disease.

Claim 72. The method as claimed in Claim 59, wherein said organism is human.

Claim 73. The method as claimed in Claim 59, wherein said disease is cancer.

AMENDMENT

U.S. Appln. No. 09/429,003

Claim 74. The method as claimed in Claim 59, wherein said cells are isolated from tissue, body fluid or body waste of said eukaryotic organism.

Claim 75. The method as claimed in Claim 74, wherein said body fluid is blood.

Claim 76. The method as claimed in Claim 59, wherein said disease is selected from the group comprising stomach, lung, breast, prostate gland, bowel and skin cancer.

Claim 77. The method as claimed in Claim 59, wherein said disease is Alzheimer's disease.

Claim 78. A method of obtaining isolated selected mRNA species or isolated selected cDNA species useful for diagnosing or identifying Alzheimer's disease or stage thereof in a human comprising the steps of:

- (a) isolating mRNA from cells of one or more humans which are known to have said disease or a stage thereof (diseased sample), wherein said cells are obtained from a part of said humans distant to the area of said disease, wherein the resulting isolated mRNA is optionally subjected to reverse transcription to obtain isolated cDNA;
- (b) isolating mRNA from corresponding cells of one or more normal humans (normal sample), wherein the resulting isolated mRNA is optionally subjected to reverse transcription to obtain isolated cDNA;
- (c) separating, by a non-sequence based separation technique, mRNA species or cDNA species present within each of the resulting isolated mRNA or

AMENDMENT

U.S. Appln. No. 09/429,003

isolated cDNA of step (a) and step (b), wherein the resulting separated mRNA species are optionally subject to reverse transcription to obtain separated cDNA species;

- Es
cont
- (d) selecting two or more mRNA species or two or more cDNA species from the resulting separated mRNA species or resulting separated cDNA species obtained in step (c), respectively, which are present at a different level in the normal sample than in the diseased sample by identifying a signal corresponding to each mRNA species or cDNA species, wherein the resulting selected two or more mRNA species are optionally subjected to reverse transcription to obtain two or more selected cDNA species; and
- (e) isolating the resulting two or more selected mRNA species or resulting two or more selected cDNA species obtained in step (d) to obtain isolated selected mRNA species or isolated selected cDNA species, wherein the resulting isolated selected mRNA species are optionally subjected to reverse transcription to obtain isolated selected cDNA species.

Claim 79. The method as claimed in Claim 78, wherein in steps (a) and (b), the resulting isolated mRNA is subjected to reverse transcription to obtain isolated cDNA.

Claim 80. The method as claimed in Claim 79, wherein said isolated cDNA is amplified.

AMENDMENT

U.S. Appln. No. 09/429,003

Claim 81. The method as claimed in Claim 78, wherein said isolated cDNA is labelled.

Claim 82. The method as claimed in Claim 78, wherein, in step (e), between 50 and 100 mRNA species or cDNA species are isolated and selected.

Claim 83. The method as claimed in Claim 78, wherein, in step (e), between 10 and 500 mRNA species or cDNA species are isolated and selected.

85 Claim 84. The method as claimed in Claim 78, wherein, in step (c), said separation technique is gel electrophoresis.

Claim 85. The method as claimed in Claim 78, wherein said cells are isolated from tissue, body fluid or body waste of said eukaryotic organism.

Claim 86. The method as claimed in Claim 85, wherein said body fluid is blood.

Claim 87. A method of preparing a gene transcript pattern probe kit comprising the steps of:

- (a) isolating mRNA from cells of one or more humans which are known to have Alzheimer's disease or a stage thereof (diseased sample), wherein said cells are obtained from a part of said humans distant to the area of said disease, wherein the resulting isolated mRNA is optionally subjected to reverse transcription to obtain isolated cDNA;
- (b) isolating mRNA from corresponding cells of one or more normal humans (normal sample), wherein the resulting isolated mRNA is optionally subjected to reverse transcription to obtain isolated cDNA;

AMENDMENT

U.S. Appln. No. 09/429,003

- Es
- (c) separating, by a non-sequence based separation technique, mRNA species or cDNA species present within each of the resulting isolated mRNA or isolated cDNA of step (a) and step (b), wherein the resulting separated mRNA species are optionally subject to reverse transcription to obtain separated cDNA species;
 - (d) selecting two or more mRNA species or two or more cDNA species from the resulting separated mRNA species or resulting separated cDNA species obtained in step (c), respectively, which are present at a different level in the normal sample than in the diseased sample by identifying a signal corresponding to each mRNA species or cDNA species, wherein the resulting selected two or more mRNA species are optionally subjected to reverse transcription to obtain two or more selected cDNA species;
 - (e) isolating the resulting two or more selected mRNA species or resulting two or more selected cDNA species obtained in step (d) to obtain isolated selected mRNA species or isolated selected cDNA species, wherein the resulting isolated selected mRNA species are optionally subjected to reverse transcription to obtain isolated selected cDNA species; and
 - (f) immobilizing the resulting isolated selected mRNA species or isolated selected cDNA species of

AMENDMENT

U.S. Appln. No. 09/429,003

step (e) on at least one solid support so as to form a gene transcript pattern probe kit.

Claim 88. The method as claimed in Claim 87, wherein, prior to immobilizing in step (f), the resulting isolated selected mRNA species or isolated selected cDNA species of step (e) are amplified.

Claim 89. The method as claimed in Claim 87, wherein said solid support is a filter.

Claim 90. A method of preparing a standard gene transcript pattern characteristic of Alzheimer's disease or stage thereof comprising the steps of:

- ES
- (a) isolating mRNA from cells of one or more humans known to have said disease or a stage thereof, wherein said cells are obtained from a part of said humans distant to the area of said disease, wherein the resulting isolated mRNA is optionally subjected to reverse transcription to obtain isolated cDNA;
 - (b) hybridizing the resulting isolated mRNA or isolated cDNA of step (a) to two or more mRNA species which are present at a different level in cells in a normal sample than corresponding cells in an Alzheimer's diseased sample, wherein the two or more mRNA species or cDNA species are specific for said disease or stage thereof and wherein said cells are obtained from a part of said human distant to the area of said disease, or to two or more cDNA species transcribed from

AMENDMENT

U.S. Appln. No. 09/429,003

- said mRNA species, wherein said mRNA or cDNA species are immobilized on a solid support; and
- (c) assessing the amount of hybridisation so as to obtain said standard gene transcript pattern.

Claim 91. A method of preparing a test gene transcript pattern for Alzheimer's disease or stage thereof comprising the steps of:

- Es
- (a) isolating mRNA from cells of a test human, wherein said cells are obtained from a part of said human distant to the area of said disease, wherein the resulting isolated mRNA is optionally subjected to reverse transcription to obtain isolated cDNA;
- (b) hybridizing the resulting isolated mRNA or isolated cDNA of step (a) to two or more mRNA species which are present at a different level in cells in a normal sample than corresponding cells in an Alzheimer's diseased sample, wherein the two or more mRNA species or cDNA species are specific for said disease or stage thereof and wherein said cells are obtained from a part of said human distant to the area of said disease, or to two or more cDNA species transcribed from said mRNA species, wherein said mRNA or cDNA species are immobilized on a solid support; and
- (c) assessing the amount of hybridization so as to obtain said test gene transcript pattern.

AMENDMENT

U.S. Appln. No. 09/429,003

Claim 92. A method of diagnosing or identifying Alzheimer's disease or stage thereof in a test human comprising the steps of:

Es

- (a) isolating mRNA from cells of a test human, wherein said cells are obtained from a part of said human distant to the area of said disease, wherein the resulting isolated mRNA is optionally subjected to reverse transcription to obtain isolated cDNA;
- (b) hybridizing the resulting isolated mRNA or isolated cDNA of step (a) to two or more mRNA species which are present at a different level in cells in a normal sample than corresponding cells in an Alzheimer's diseased sample, wherein the two or more mRNA species or cDNA species are specific for said disease or stage thereof and are obtained from a part of said human distant to the area of said disease, or to two or more cDNA species transcribed from said mRNA species, wherein said mRNA or cDNA species are immobilized on a solid support;
- (c) assessing the amount of hybridization so as to obtain a hybridization pattern;
- (d) comparing the resulting hybridization pattern obtained in step (c) with a hybridization pattern obtained by hybridizing isolated mRNA or isolated cDNA prepared from corresponding cells from one or more humans known to have said disease or